



Case Report

A case of premature ventricular contractions, ventricular tachycardia, and arrhythmic storm induced by right ventricular pacing during cardiac resynchronization therapy: Electrophysiological mechanism and catheter ablation



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ABSTRACT

A 77-year-old man with ischemic cardiomyopathy and a cardiac resynchronization therapy-defibrillator (CRT-D) device came to our attention due to incessant ventricular tachycardia and multiple implantable cardioverter defibrillator (ICD) shocks. An electrocardiogram showed non-sustained monomorphic ventricular tachycardias (NSVTs) constantly occurring after each biventricular stimulation. During an electrophysiological study, NSVTs reproducibly recurred only after right ventricular (RV) pacing; LV pacing did not induce any NSVTs.

The activation map was consistent with a localized reentry at the interventricular septum, and a double exit; at the LV exit site, a single radiofrequency energy application immediately interrupted the occurrence of the NSVTs.

Current evidence supports LV pacing to be pro-arrhythmogenic in few CRT patients. This unusual case shows that RV pacing during CRT could produce frequent ventricular arrhythmias and arrhythmic storm. Catheter ablation can be considered an effective therapeutic option, especially when CRT maintenance is highly advisable.

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1. Introduction

Left ventricular pacing (LVP) has been recognized as a rare trigger of ventricular arrhythmias after cardiac resynchronization therapy (CRT) [1]. In general, such events arise early after implantation, while a late occurrence has been reported only once, in a patient with ischemic cardiomyopathy suffering from LVP-induced ventricular tachycardia (VT) storm 7 years after CRT initiation [2].

The pathophysiology of LVP-induced VTs remains controversial. The leading theory relies on enhanced transmural dispersion of repolarization during LVP [3]; recently, a reentrant mechanism involving an epicardial scar was demonstrated in a small group of patients with early electrical storm after CRT onset, in which catheter ablation resulted in complete resolution of the condition and safe CRT resumption [4].

We describe a case of right-ventricular pacing (RVP)-induced VTs along with the possible mechanism of the arrhythmia, eventually

causing an arrhythmic storm, in a patient with previous myocardial infarction and CRT.

2. Case report

A 77-year-old man with ischemic dilated cardiomyopathy and a previous anterior myocardial infarction came to our attention due to incessant ventricular tachycardia and multiple implantable cardioverter defibrillator (ICD) shocks.

The patient was affected by dilated cardiomyopathy with an apical aneurysm, severe left-ventricular (LV) systolic impairment, a complete left bundle branch block (LBBB), a chronic total occlusion of the left descending coronary artery, and severe stenosis of the right coronary artery. An atrioventricular defibrillator had been implanted in 2006 following resuscitation from a cardiac arrest, with a passive fixation, dual-coil implantable cardioverter defibrillator (ICD) lead (Sprint Fidelis[®], Medtronic Inc., Minneapolis, MN, US) positioned at the mid-apical right ventricular (RV) septum.

The subsequent implant follow-up was uneventful. Elective replacement of the device was performed in 2009 and again in March 2014; the leads were performing well and were regularly

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connected to the new device (VIVA XT CRT-D, Medtronic Inc., Minneapolis, MN, US); the ICD programming was left unchanged.

A few weeks after the last replacement, multiple ICD shocks occurred. A device interrogation revealed non-sustained fast monomorphic ventricular tachycardias (NSVTs) incessantly recurring after a few biventricular paced beats; ICD therapies with anti-tachycardia pacing (ATP) and direct current shocks (DCSs) were either ineffective or inappropriately delivered after spontaneous interruption.

After the initial evaluation, which excluded acute ischemia, electrolyte imbalance, and other common transient precipitating factors, stabilization was achieved with sedation and intravenous amiodarone. Subsequently, a recurrence of slower, short NSVTs occurred. Of note, each biventricular stimulation was reproducibly followed by three monomorphic ventricular complexes (Fig. 1A).

The NSVTs showed an LBBB morphology with superior and right axis deviation and negative concordance in the precordial leads, which is indicative of inferoapical septal origin. Suspecting a pacing-induced triggered mechanism, biventricular pacing (BiVP) was temporarily suspended, which was followed by the immediate cessation of the NSVTs. Subsequently, RVP only, LVP only, or BiVP were unable to reinduce the NSVTs.

A VT ablation procedure was scheduled. The procedure was conducted in a fasting state under general anesthesia with mechanical ventilation. The presence of intraventricular thrombus was excluded using echocardiography. The pre-specified procedural end-points were the non-inducibility of sustained monomorphic VTs and substrate modification by means of the elimination of late potentials (LPs). As previously described [5], an LP was defined as an isolated bipolar potential occurring after the end of the surface QRS (either spontaneous or paced), which was separated from the main ventricular potential by an isoelectric tract.

A quadripolar mapping catheter was placed along the RV septum, and a 3.5 mm bidirectional open irrigated mapping catheter (ThermoCool SF[®], Biosense Webster, Johnson's & Johnson's, Diamond Bar, CA, US) was inserted retrogradely into the LV. An electroanatomical substrate map created using the CARTO3[®] system (Biosense Webster, Johnson's & Johnson's, Diamond Bar, CA, US) was obtained during constant sinus-triggered LVP (via the

LV device lead). Pacing was necessary due to the absence of a spontaneous ventricular rhythm; LVP was preferred to enhance delayed septal activation. Thresholds for the bipolar substrate map were set at 1.5 mV and 0.5 mV to discriminate respectively healthy tissue and “dense” scar, as is typically set up for ventricular substrate mapping.

A large area of the anterior, septal, and apical scar was reconstructed without evident LPs. The RV substrate map revealed low amplitude potentials at the apical septum, again without LPs (Fig. 2a, b).

Inducibility was tested with programmed LV stimulation first, without the induction of any sustained arrhythmias. RV pacing was then initiated, but the induction protocol was immediately stopped since a regular recurrence of the NSVTs following one or two paced complexes appeared, with the same morphology that had been encountered clinically.

Changing the site of RV septal pacing did not influence the NSVT occurrence or morphology, despite a different interval between the spike and NSVT onset; reproducibility was demonstrated by temporary switching to LV stimulation (Fig. 1B). Notably, the ICD bipolar morphology (tip-ring) of the NSVTs closely matched the clinical VTs (see Supplemental material, SM1).

A biventricular activation map of the induced NSVTs was then performed, which confirmed a centrifugal activation originating from the infero-apical interventricular septum to both ventricles (see Fig. 2c) without significant anticipation on both sides of the septum. The best pacemap QRS concordance was 11/12 on both sides of the septum (a discordant V1 is evident; see Supplemental material, SM2); a unipolar electrogram was also suboptimal for ectopic origin at the same sites.

Initial ablation attempts of a putative intramural source of NSVTs, where the best pacemap or best unipolar electrograms were present, failed to interrupt the arrhythmias, despite the high power and irrigation rate on both the RV and the LV sides of the septum.

Further careful mapping at the LV exit allowed to find a single site showing a late potential after a paced RV complex, followed by a low-amplitude, highly fragmented diastolic potential occurring 90 ms before the NSVT onset (Fig. 3). At this site, a single radio-frequency (RF) energy application interrupted the occurrence of

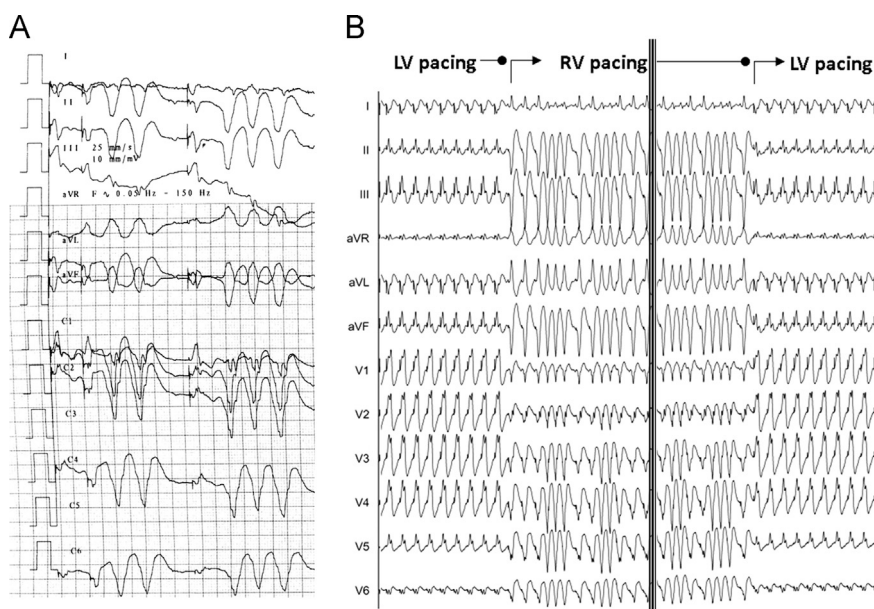


Fig. 1. (A) A 12-lead surface electrocardiogram showing biventricular pacing-induced non-sustained ventricular tachycardias (NSVTs). (B) Demonstration of the NSVTs' dependency on right ventricular pacing (RVP) during an electrophysiological study. The shift from left ventricular pacing (LVP) to RVP is followed by the immediate induction of NSVTs; the NSVTs are suddenly abolished after the pacing site has been shifted again to LVP.

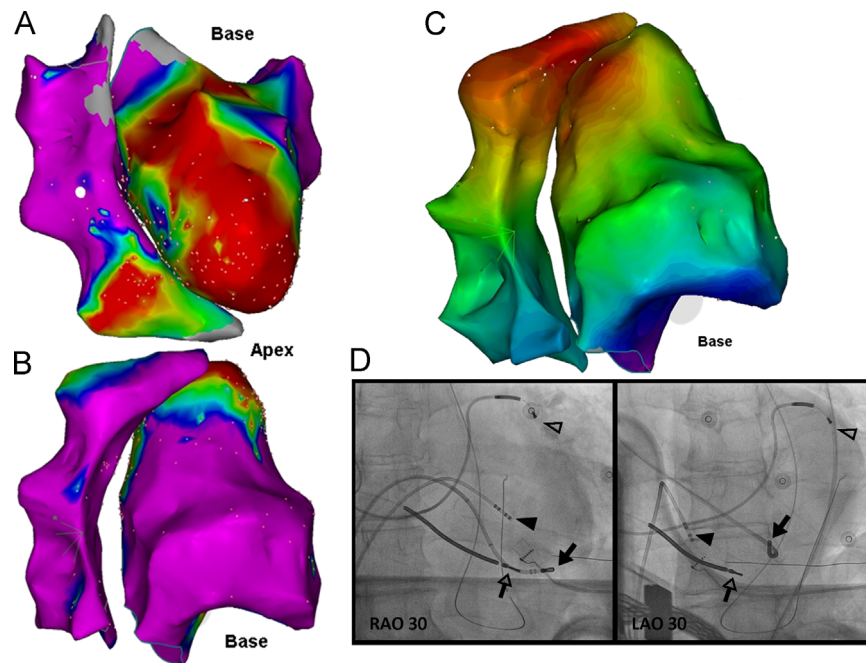


Fig. 2. An electroanatomic bipolar voltage map of the left and right ventricle during left ventricular pacing (LVP). (A) Superior view. A large anteroseptal and apical infarction is evident, with extension to the anterior right ventricular (RV) apex. (B) Inferior view. Inferoseptal potentials are relatively preserved. (C) Inferior view. Biventricular activation map of non-sustained ventricular tachycardias (NSVTs: the second complex of NSVT was mapped): a centrifugal activation coming from the inferior apical septum is demonstrated, without significant anticipation at both sides of the septum. The isochronal steps are set at 5 ms. (D) Fluoroscopic 30° right anterior oblique (RAO 30) and 30° left anterior oblique (LAO 30) projections of the mapping catheter at the earliest RV activation site and at the successful left ventricular (LV) ablation site, respectively. The mapping catheter position relative to the implantable cardioverter defibrillator (ICD) lead and the RV quadripolar diagnostic catheter can be appreciated. Arrow: ICD lead; arrowhead: LVP catheter; solid arrow: mapping/ablation catheter; solid arrowhead: quadripolar RV mapping catheter.

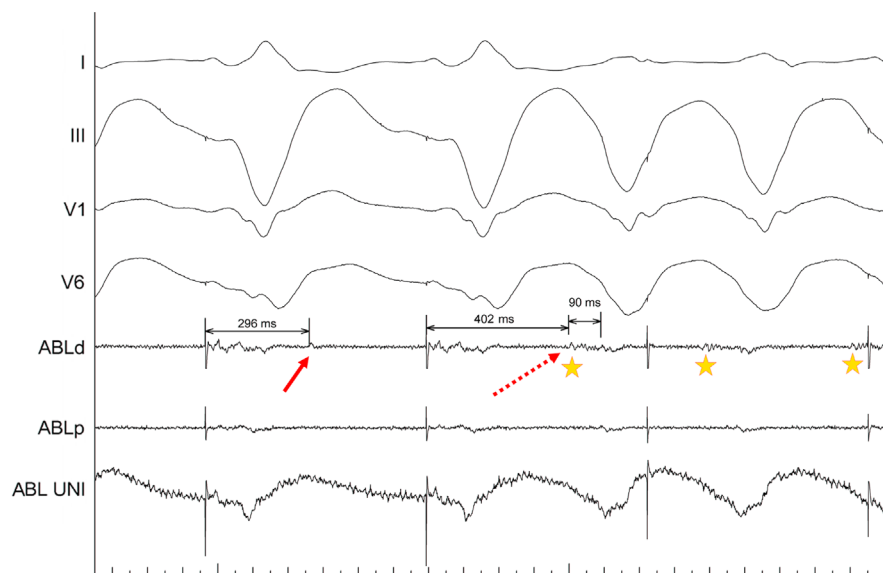


Fig. 3. Local bipolar signal at the effective ablation site. After a non-inducing right ventricular pacing (RVP), a local prolonged and fragmented activation is recorded; about 300 ms after the stimulus, a delayed potential occurs (red arrow). After an inducing RVP, the same local prolonged and fragmented activation is unchanged; the delayed potential is shifted 106 ms forward, and a prolonged, fragmented activation with fair specularity follows to produce the first surface premature ventricular contraction (PVC); all subsequent PVCs are preceded by identical diastolic potentials (yellow stars), preceding the QRS onset by 90 ms.

NSVTs after 4.6 s (see [Supplemental material, SM3](#)); at the end of the RF application, a very late potential was recorded at the same site (see [Supplemental material, SM4](#)).

After 30 min, non-inducibility was confirmed by multisite RV pacing, and the procedure was concluded. The subsequent hospital stay was uneventful, except for the occurrence of atrial fibrillation, which was treated with external cardioversion. A predischarge device check revealed a nearly complete abolition of ventricular extra beats, with a substantial increase of the CRT stimulation rate.

The patient remained free from recurrence in the following 3 months.

3. Discussion

This is the first report of a late onset of recurrent NSVTs and arrhythmic storm caused by RV pacing by a CRT device, and it describes a possible underlying electrophysiological mechanism.

It has been already evidenced that RV backup pacing in patients implanted with an ICD can rarely induce VT [6], with an association between the RVP rate and the induced VT risk. However, the negative influence of chronic RV pacing on ventricular function might have worsened the arrhythmic burden in these patients as well as influencing the progression of heart failure symptoms.

Ventricular tachycardia associated with structural heart disease is generally macroreentrant in nature, around or within areas of slow conduction characterizing diseased tissue, as in the case of myocardial infarction. Enhanced automaticity and triggered activity have been seldom observed outside of the context of acute ischemia, decompensation, electrolyte imbalance, acidosis, inotropic therapy, or other transient triggering factors.

Our findings are highly suggestive of a concealed localized reentry, with unidirectional block and double exit as the underlying mechanism established in conjunction with the progression of the myocardial disease. We propose a possible schematic explanation of the arrhythmia mechanism in Fig. 4.

In the presence of anteroseptal myocardial infarction, the localized reentry is most probably closer to the left side of the septum, while the true RV exit is most likely intramural. We can speculate that conduction occurred through a complex, three-dimensional architecture of healthy and fibrotic tissue while approaching the RV endocardial breakthrough; in such a situation, conduction was probably highly anisotropic, so that the earliest endocardial RV activation would have been located at a considerable distance from the intramural exit. This distance could explain why ablation at the RV endocardial breakthrough failed to abolish or modify the NSVTs; furthermore, catheter stability and contact force might have been suboptimal to allow efficacy.

Localized reentry has been suggested for idiopathic VTs arising in the Purkinje network [7]. Concerning structural heart disease, possible localized, re-entrant VTs have been reported in RV arrhythmogenic cardiomyopathy [8] and in experimental

infarctions [9]; however, continuous electrical activity has also been recorded at successful RF ablation sites in those cases. Therefore, a functional nature of reentry cannot be excluded.

We did not observe continuous electrical activity at the RF ablation site. Although we cannot exclude that this could have been precluded by the deep location of the circuit in the myocardial septum, the evidence supporting a dual conduction physiopathology favors the anatomical nature and discrete dimension of a reentry circuit rather than a functional explanation.

Finally, a few adjunctive observations can be obtained from this case: (1) double exit at both sides of a relatively thick myocardial wall might explain a suboptimal pacemap; (2) arrhythmogenic electrical activity (LPs) at the target sites might be missed when mapping takes place during sinus rhythm or ventricular pacing; (3) a localized “protected” reentry might explain failure of VT interruption with ATP.

3.1. Limitations

We could not induce sustained VTs to demonstrate the same mechanism of NSVTs; for the same reason, no responses to resetting and entrainment maneuvers were observed. This might limit the generalization of the proposed mechanism. We also could not explain the high variability in the inducibility and duration of NSVTs or the cause of such a late arrhythmic manifestation.

4. Conclusions

This clinical picture shows that ventricular arrhythmias with apparent triggered behavior may be dependent upon a localized reentrant mechanism. This fact should be considered in analog cases in order to tailor appropriate pharmacologic and interventional therapies. Changing the pacing setup, together with

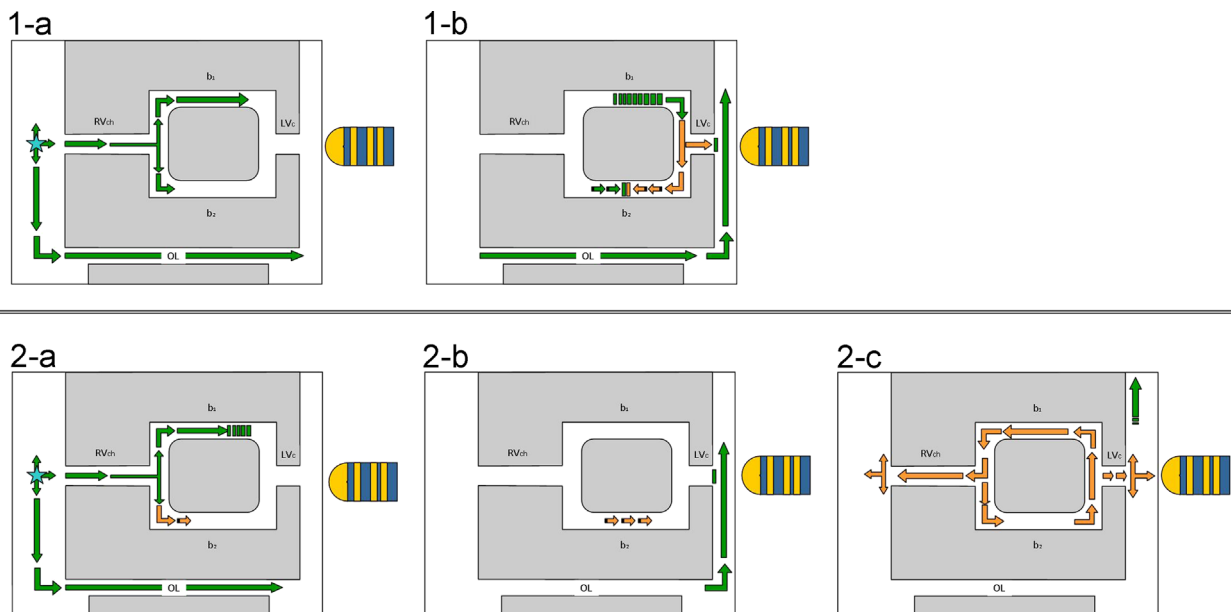


Fig. 4. Schematic explanation of the proposed mechanism of pacing-induced (non-sustained ventricular tachycardias (NSVTs)). An intramural loop constituted by two conducting bundles (b1, b2) with different refractoriness and conduction velocity is outlined. The circuit is connected to both ventricles by slow conducting channels (right ventricle channel (RVch), left ventricle channel (LVch)); the LVch is supposed to have a mechanism to allow only unidirectional, slow conduction towards the LV. The gray areas represent non-conducting tissue. The blue star indicates the site of RV stimulation; the position of the mapping catheter is also shown at the LVch exit. 1-(a) Activation of a non-inducing RV paced beat: activation proceeds along both an outer loop (OL) and b1 (with faster conduction and longer refractoriness), giving rise to a late potential (LP); LVch activation finds the myocardium at the LVch exit already activated by the outer loop, so that a functional block is established. 1-(b) Activation of b2 proceeds both antegradely and retrogradely. 2-(a) An inducing beat propagates along the outer and inner loop as well but finds b1 still refractory; 2-(b) activation occurs along b2 (bundle with slower conduction and shorter refractoriness), generating a shifted delayed potential; 2-(c) having recovered its excitability, the LV can now be activated via the LVch; retrograde propagation proceeds as well through the fast b1 bundle and to the RV exit site; b2 is again excitable due to its short refractoriness, allowing the perpetuation of reentry.

antiarrhythmic therapy, might suppress pacing-induced NSVTs, which would produce immediate symptom relief, hemodynamic improvement, and possibly limitation of recurrences in the short term.

If confirmed in other cases, these findings could support catheter ablation as the treatment of choice in pacing-induced NSVTs. This option would be particularly useful in CRT responders in whom BiVP suspension might be hazardous because of its unpredictable functional deterioration and worsening heart failure.

Conflict of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.joa.2015.06.002>.

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